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Section 1 - Identification

- (a) **Product Identifier:** Midazolam Injection, USP (5 mg/mL) with preservative
- (b) **Product Code:** 70860-601
 - Common/Trade Name:** Midazolam Hydrochloride, Midazolam Injection
 - Chemical Name:** 8-chloro-6-(2-fluorophenyl)-1-methyl-4*H*-imidazo[1,5-a][1,4]benzodiazepine hydrochloride
 - Chemical Family:** Benzodiazepine
- (c) **Product Use:** Pharmaceutical, Injectable
 - Product Type:** Regulated Prescription Drug
 - Container Information:** Vials
- (d) **Distributor:** Athenex Pharmaceutical Division, 10 N. Martingale Road, Suite 230, Schaumburg, IL 60173, 847-886-9515
- (e) **Emergency Telephone:** 855-273-0154


Section 2 - Hazards Identification

- (a) **Classification:**
 - US OSHA Classification:** Target Organ Toxin, Reproductive Toxin

HMIS Rating

Health Hazard	2
Fire Hazard	1
Reactivity Hazard	1

(b) Signal Word, Hazard statement(s), Symbol(s), and/or Precautionary statement(s):	(c) Description of Hazards:
GHS Hazard Statements	
- Not Available	

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(b) Signal Word, Hazard statement(s), Symbol(s), and/or Precautionary statement(s):	(c) Description of Hazards:
P201 P202 P280.2 P281	<p><u>GHS Precautionary Statements</u></p> <p>PREVENTION</p> <ul style="list-style-type: none"> - Obtain special instructions before use - Do not handle until all safety precautions have been read and understood - Wear protective gloves and eye/face protection - Use personal protective equipment as required <p>RESPONSE</p> <ul style="list-style-type: none"> - If exposed or concerned: Get medical attention - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical attention. Wash hands after handling.

(d)
Unknown Acute Toxicity N/A

Section 3 – Composition / Information on Ingredients

Midazolam Hydrochloride Injection (with preservative, multi-dose):
 5 mg/mL (5 mL and 10 mL)

(a) Chemical Name	(b) Common Name / Synonym	% Composition or other measure 5 mL fill	% Composition or other measure 10 mL fill	(c) CAS No.	(d) Impurities/ Stabilizing Additives
8-chloro-6-(2-fluorophenyl)-1-methyl-4H-imidazo[1,5-a][1,4]benzodiazepine	Midazolam Hydrochloride	25.0 mg/unit	50.0 mg/unit	59467-96-8	N/A
Phenylmethanol	Benzyl Alcohol	50.0 mg/unit	100.0 mg/unit	100-51-6	N/A

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(a) Chemical Name	(b) Common Name / Synonym	% Composition or other measure 5 mL fill	% Composition or other measure 10 mL fill	(c) CAS No.	(d) Impurities/ Stabilizing Additives
Sodium Chloride	Sodium Chloride	40.0 mg/unit	80.0 mg/unit	7647-14-5	N/A
Hydrochloric Acid	Hydrochloric Acid	q.s. to pH adjustment	q.s. to pH adjustment	7647-01-0	N/A
Sodium Hydroxide	Sodium Hydroxide	q.s. to pH adjustment	q.s. to pH adjustment	1310-73-2	N/A
Disodium 2,2'-{1,2-ethanediylbis [(carboxymethyl)imino]} diacetate	Edetate Disodium	0.5 mg/unit	1.0 mg/unit	6381-92-6	N/A
Water	Water for Injection	q.s. to 5 mL	q.s. to 10 mL	7732-18-5	N/A
0.1N Hydrochloric Acid	0.1N Hydrochloric Acid	1.15 mL/unit	2.30 mL/unit	7647-01-0	N/A

Section 4 - First Aid Measures

- Eye Exposure:** Immediately flush eyes with water for at least 15 minutes. Seek medical attention.
- Skin Exposure:** Remove contaminated clothing immediately. Flush area with water for at least 15 minutes. Seek medical attention.
- Ingestion:** Do not induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Seek medical attention.
- Injection:** See patient package insert in shipping carton for complete information.
- Inhalation:** Move exposed subject to fresh air immediately. Give artificial respiration and cardiopulmonary resuscitation (CPR) if required. Seek medical attention.
- Notes to Physician:** See patient package insert in shipping carton for complete information.

Section 5 –Fire-fighting Measures

- (a) Extinguishing Media** Water spray, dry chemical, carbon dioxide, or foam as appropriate to surroundings.

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- (b) **Hazardous Combustion Products:** When heated to decomposition, toxic fumes may be emitted.
- (c) **Special Protective Equipment / Precautions:** Wear self-containing breathing apparatus and protective clothing.

Section 6 - Accidental Release Measures

- Spill:** Wear recommended personnel protective equipment (See Section 8 – Exposure Controls/Personal Protection). Use absorbent towels or brooms to clean-up spill. Wipe surface area clean with soap and water.
- Release to Air:** If aerosolized, reduce exposures by ventilating the area; clean up spill immediately to prevent evaporation
- Release to Water:** Refer to local water authority. Drain disposal is not recommended; refer to local, state, and federal disposal guidelines.

Section 7 - Handling and Storage


- General Handling:** When handling pharmaceutical products, avoid all contact and inhalation of dust, fumes, mist, and/or vapors associated with product.
- Storage Conditions:** Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature]. Follow instructions provided in packaging.

Section 8 - Exposure Controls / Personal Protection

(a) **Exposure Limits**

(b)

Compound	Issuer	Type	Exposure Limit
Midazolam Hydrochloride	OSHA	PEL	NE
	ACGIH	TLV	NE
	----	STEL	NE
Sodium Chloride	OSHA	PEL	NE
	ACGIH	TLV	NE
	----	STEL	NE
Edetate Disodium	OSHA	PEL	NE
	ACGIH	TLV	NE
	----	STEL	NE
Benzyl Alcohol	OSHA	PEL	NE

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	ACGIH -----	TLV STEL	NE NE
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(c) Engineering Controls


Ventilation: Handle product in a well-ventilated area

(d) Individual Protection Measures

Respiratory Protection:	<p>With satisfactory ventilation, respiratory protection is usually not required.</p> <p>However, if the generation of aerosols is likely, and engineering controls are not considered adequate to control potential airborne exposures, the use of an approved air-purifying respirator with a HEPA cartridge (N99 or equivalent) is recommended under conditions where airborne aerosol concentrations are not expected to be excessive. For uncontrolled release events, or if exposure levels are not known, provide respirators that offer a high protection factor such as a powered air purifying respirator or supplied air.</p>
Eye Protection:	Safety glasses or goggles recommended.
Skin Protection:	Disposable garments if direct skin contact is anticipated.
Other Protective Equipment:	Disposable latex gloves are recommended.
Additional Exposure Precautions:	None established.

Section 9 - Physical and Chemical Properties

(a) Appearance	Clear, colorless to light yellow solution
(b) Odor	Not available
(c) Odor Threshold	Not available
(d) pH	2.5 – 3.5
(e) Melting Point:	Not available
(f) Initial Boiling Point:	159 °C

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(g)	Flash Point	Not available
(h)	Evaporation Rate:	Not available
(i)	Flammability	Not available
(j)	Upper Lower Flammability or Explosion Limits	Not available
(k)	Vapor Pressure:	Not available
(l)	Vapor Density:	Not available
(m)	Relative Density	Not available
(n)	Solubility(ies)	Soluble in Water
(o)	Partition Coefficient: n-octanol/water	Not available
(p)	Auto-ignition Temperature	Not available
(q)	Decomposition Temperature	Not available
(r)	Viscosity	Not available

Section 10 - Stability and Reactivity

(a)	Reactivity	Not Available
(b)	Chemical Stability	Stable
(c)	Possibility of Hazardous Reactions	Hazardous polymerization will not occur
(d)	Conditions to Avoid	Slightly reactive with oxidizing agents
(e)	Incompatible Materials	Store away from strong oxidizers
(f)	Hazardous Decomposition Products	As with any burning material, carbon monoxide, nitrogen oxides, and sulfur oxides may be produced. Also, fluorine and chlorine gases could be produced.

Section 11 - Toxicological Information


(a)	Likely Routes of Exposure	Inhalation, eye/skin contact, or ingestion
(b)	Symptoms related to the physical, chemical and toxicological characteristics	This product is intended for therapeutic use only when prescribed by a physician. Potential adverse reactions from prescribed doses and overdoses are described in the package insert. Adverse reactions from therapeutic doses include: respiratory depression, respiratory arrest, airway obstruction, oxygen desaturation, apnea, cardiac arrest, hypotensive episodes,

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(b)	Symptoms related to the physical, chemical and toxicological characteristics	<p>agitation, involuntary movements, hyperactivity, combativeness, headache, hiccoughs, nausea, vomiting, coughing, oversedation, and drowsiness. Occupational exposure has not been fully investigated.</p> <p>NOTE: This product is classified by the Controlled Substances Act as a Schedule IV controlled substance. Abuse of this product may lead to limited physical dependence or psychological dependence.</p>
(c)	Delayed and immediate effects and also chronic effects from short and long term exposure	<p>During occupational use, this product should be considered potentially irritating to the eyes and respiratory tract. IN clinical use, common adverse effects include drowsiness, sedation, muscle weakness, and ataxia. Less frequent adverse effects include vertigo, headache, confusion, depression, slurred speech, tremor, visual disturbances, urinary retention or incontinence, gastrointestinal disturbances, decreased blood pressure, changes in salivation, and amnesia.</p>

(e) Acute Toxicity

Component	Type	Route	Species	Dosage
Midazolam Hydrochloride	LD ₅₀	Oral	Rat	1600 mg/kg
Benzyl Alcohol	LD ₅₀	Skin	Rabbit	2000 mg/kg
Benzyl Alcohol	LD ₅₀	Skin	Rat	100 pph/90 minutes
Benzyl Alcohol	LC ₅₀	Inhalation	Mouse	>500 mg/m ³
Benzyl Alcohol	LC ₅₀	Inhalation	Rat	>500 mg/m ³
Benzyl Alcohol	LD ₅₀	Oral	Mouse	1360 mg/kg
Benzyl Alcohol	LD ₅₀	Oral	Rat	1230 mg/kg
Benzyl Alcohol	LD ₅₀	Intravenous	Rat	53 mg/kg
Benzyl Alcohol	LD ₅₀	Intravenous	Mouse	324 mg/kg
Benzyl Alcohol	LD ₅₀	Intraperitoneal	Rat	400 mg/kg
Benzyl Alcohol	LD ₅₀	Intraperitoneal	Mouse	650 mg/kg
Edetate Disodium	LD ₅₀	Oral	Rat	2.0 -3.7 g/kg
Edetate Disodium	LD ₅₀	Oral	Mouse	400 mg/kg

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Component	Type	Route	Species	Dosage
Sodium Chloride	LD ₅₀	Skin	Rabbit	>10 g/kg
Sodium Chloride	LC ₅₀	Inhalation	Rat	>42g/m ³ in 1hr
Sodium Chloride	LD ₅₀	Intravenous	Mouse	645 mg/kg
Sodium Chloride	LD ₅₀	Intraperitoneal	Mouse	2602 mg/kg
Sodium Chloride	LD ₅₀	Intraperitoneal	Rat	2600 mg/kg
Sodium Chloride	LD ₅₀	Subcutaneous	Mouse	3 mg/kg

Immediate Effects: Eye, skin, and respiratory irritation have been experienced with patient administration.

(f) Hazardous Chemical Listings


NTP: Not Available

IARC: Not Available

OSHA: Not Available

Section 12 - Ecological Information

		<p>Not determined for the product. Information for ingredients is as follows:</p> <p><u>Midazolam Hydrochloride</u> LC50(48hr) = 7.1 mg/l in Daphnia EbC50(72hr) = 11.4 mg/l in algae (the no-observable biological effect concentration on growth (72hr) was 3.7 mg/l). LC50 = 4.3 mg/L in rainbow trout</p> <p><u>Benzyl Alcohol</u> EC50 (Water flea) = 23 mg/L LC50 (96hr, fathead minnow, 18-22°C) = 460 mg/L LC50 (96hr, bluegill) = 10 mg/L</p> <p>LC50 (96hr, Pimephales promelas) = 460 mg/L LC50 (Leuciscus idus) = 640 mg/L EC50 (24hr, Daphnia magna) = 400 mg/L EC50 (Chlorella pyrenoidosa) = 95 mg/L EC50 (Photobacterium phosphoreum) = 63.7 to 71.4 mg/L</p>
(a)	Ecotoxicity	
(b)	Persistence and degradability	Not determined for the product. Information for

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		ingredients is as follows: Midazolam was only 6% biodegraded in 28 days in the Sturm test. The EC50 (3h) for inhibition of microbial respiration was greater than 100 mg/l indicating that this material was non- inhibitory to microorganisms in the activated sludge respiration inhibition test.
(c)	Bioaccumulative potential	Not available
(d)	Mobility in soil	Not available
(e)	Other Adverse Effects	Not available

Section 13 - Disposal Considerations

Waste Disposal: Dispose of any cleanup materials and waste residue according to all applicable laws and regulations.


Section 14 - Transport Information

(a)	UN Number	Not available
(b)	UN Proper Shipping Name	Not available
(c)	Transport Hazard Class(es)	Not available
(d)	Packing Group	Not available
(e)	Environmental Hazards	Not available
(f)	Transport in bulk (according to Annex II of MARPOL 73/78 and the IBC Code)	Not available
(g)	Special Precautions	Not available

DOT: Not Regulated
ICAO/IATA: Not Regulated
IMO: Not Regulated

Section 15 - Regulatory Information

Below is selected regulatory information chosen primarily for possible Athenex Pharmaceutical Division usage. This section is not a complete analysis or reference to all applicable regulatory information. Please consider all applicable laws and regulations for your country/state.

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U.S. Regulations:

TSCA – Benzyl Alcohol, Edetate Disodium, and Sodium Chloride are listed
 CERCLA - Not on this list
 SARA 302 - Not on this list
 SARA 313 - Not on this list
 OSHA Substance Specific - No
 California Proposition 65 – Midazolam Hydrochloride is listed (developmental)

Section 16 - Other Information


As of the date of issuance, we are providing available information relevant to the handling of this material in the workplace. All information contained herein is offered with the good faith belief that it is accurate. THIS SAFETY DATA SHEET SHALL NOT BE DEEMED TO CREATE ANY WARRANTY OF ANY KIND (INCLUDING WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE). In the event of an adverse incident associated with this material, this safety data sheet is not intended to be a substitute for consultation with appropriately trained personnel. Nor is this safety data sheet intended to be a substitute for product literature which may accompany the finished product.

For additional information contact:

Athenex Pharmaceutical Division
 10 N. Martingale Road, Suite 230
 Schaumburg, IL 60173
 847-886-9515

Glossary: This glossary contains definitions of general terms used in SDSs. Not all of these Glossary Terms will apply to this SDS.

ACGIH	American Conference of Governmental Industrial Hygienists
AICS	Australian Inventory of Chemical Substances
AIHA	American Industrial Hygiene Association
ANSI	American National Standards Institute
CAS Number	Chemical Abstract Service Registry Number
CERCLA	Comprehensive Environmental Response Compensation and Liability Act (of 1980)
CHAN	Chemical Hazard Alert Notice
CHEMTREC	Chemical Transportation Emergency Center
DOT	Department of Transportation
DSL	Domestic Substances List
ECHA	European Chemicals Agency
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of Notified Chemical Substances
EPA	Environmental Protection Agency
GHS	Globally Harmonized System of Classification and Labelling of Chemicals

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HEPA	High Efficiency Particulate Air (Filter)
HMIS	Hazardous Materials Identification System
IARC	International Agency for Research on Cancer
ICAO/IATA	International Civil Aviation Organization/International Air Transport Association
IMDG	International Maritime Dangerous Goods
IMO	International Maritime Organization
KOW	Octanol/Water Partition Coefficient
LEL	Lower Explosive Limit
MSDS	Material Safety Data Sheet
MSHA	Mine Safety and Health Administration
NA	Not Applicable, except in Section 14 where NA = North America
NE	Not Established
NADA	New Animal Drug Application
NAIF	No Applicable Information Found
NCI	National Cancer Institute
NDSL	Non-Domestic Substances List
NFPA	National Fire Protection Association
NIOSH	National Institute for Occupational Safety and Health
NPDES	National Pollutant Discharge Elimination System
NOS	Not Otherwise Specified
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
OEL	Occupational Exposure Limit
PEL	Permissible Exposure Limit (OSHA)
RCRA	Resource Conservation and Recovery Act
RQ	Reportable Quantity
RTECS	Registry of Toxic Effects of Chemical Substances
SARA	Superfund Amendments and Reauthorization Act
SDS	Safety Data Sheet
STEL	Short Term Exposure Limit
TLV	Threshold Limit Value (ACGIH)
TPQ	Threshold Planning Quantity
TSCA	Toxic Substances Control Act
TWA	Time Weighted Average/8 Hours Unless Otherwise Noted
UEL	Upper Explosive Limit
UN	United Nations
USP	United States Pharmacopeia
WEEL	Workplace Environmental Exposure Level (AIHA)
WHMIS	Workplace Hazardous Materials Information System

Signature Manifest

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Revision: 01

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All dates and times are in Eastern Standard Time.

SDS006

Change Request

Name/Signature	Title	Date	Meaning/Reason
Michael Scribner (MSCRIBNER)	CORPORATE QA MANAGER	24 Jan 2017, 04:32:06 PM	Approved

Dept Approval

Name/Signature	Title	Date	Meaning/Reason
Tom Moutvic (TMOUTVIC)	VP of Regulatory Affairs	25 Jan 2017, 03:06:33 PM	Approved

Final QA Approval/Set Effective Date

Name/Signature	Title	Date	Meaning/Reason
Sheila Moran (SMORAN)	VP of Quality Assurance	26 Jan 2017, 11:07:06 AM	Approved